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Preface

In July 2010 the Swedish government commissioned the Swedish Chemicals Agency (KemI) to investigate the need as well as possible conditions for a national ban on bisphenol A (BPA) in certain plastic products. The investigation was carried out in collaboration with the Swedish Food Administration (SLV). As part of the investigation KemI asked the Institute of Environmental Medicine (IMM) at Karolinska Institutet to review and evaluate the available scientific literature on exposure to BPA from different products. This report presents the results of that review.

The purpose of this report is to summarize information on potential sources of exposure to BPA in the general population. Available scientific literature relevant to the investigation, as well as risk assessment documents from different authorities and expert groups was reviewed. Additional expertise concerning dermal uptake and exposure has been kindly provided by Professor Gunnar Johanson at IMM.

Some conclusions about which exposure sources seem to be the most significant are made. However, it is beyond the scope of this investigation to provide a complete exposure assessment for BPA. Data gaps and future research needs are presented.

Contents

1. Introduction

The purpose of this report is to summarize information on potential sources of Bisphenol A (BPA) exposure available from the published literature. Information has also been gathered from risk assessments of BPA conducted by different authorities and expert groups.

BPA is a high production-volume industrial chemical. It is mainly used to manufacture polycarbonate plastics and epoxy resins. According to industry about 3.8 million tons BPA were produced worldwide in 2006 (Plastics Europe, 2007).

Polycarbonate is a polymer of BPA and makes a hard, clear and shatter-proof plastic. Polycarbonate is used to a great extent in optical media, like CDs and DVDs, in electrical and electronic equipment and in the building and automotive industries. It is also used in medical and health care equipment, as well as in the production of food packaging and bottles.

Epoxy resins also have a wide range of applications. They are commonly used in construction in the form of protective and powder coatings. Other uses include electrical and electronic equipment, civil engineering, can and coil coatings and automotive coatings.

See Appendix I for a detailed summary of BPA applications.

Exposure to BPA from polycarbonate and epoxy polymers occurs if the BPA monomer is released from these materials. This may occur as a result of incomplete polymerization or hydrolysis due to elevated temperature or extreme pH (ECB, 2008). BPA is also present in powder form on the surface of certain types of thermal printing paper, e.g. used in some cashier's receipts, from which it may readily be transferred to the skin (Biedermann *et al*., 2010).

It is generally believed that consumer exposure occurs primarily via food in contact with BPA-containing materials, such as polycarbonate baby bottles, tableware and food containers as well as food and beverage cans lined with epoxy resins. Measured concentrations of BPA in human blood, urine and other tissues confirm that exposure is widespread in the human population (Vandenberg *et al*., 2007; Calafat *et al*., 2008).

A tolerable daily intake (TDI) of 50 µg BPA/kg bodyweight (bw) has been established by the European Food Safety Authority (EFSA, 2006). However, the sufficiency of this TDI has been questioned by scientists and others. The TDI is based on the results from two multigeneration reproduction studies in rats and mice (Tyl *et al*., 2002 and 2008) where adverse effects were only observed at doses above 5 mg per kg bodyweight and day. These studies were carried out according to regulatory test guidelines and are generally considered to be of very good quality and reliable. However, there is a large amount of non-guideline studies available reporting effects of BPA exposure at doses well below 5 mg/kg bw/day, sometimes around only a few

µg/kg bw/day (reviewed in Richter *et al*., 2007). This so called "low dose controversy" has made the risk assessment of BPA particularly difficult (Beronius *et al*., 2010).

2. Estimations of exposure in the general population

Several health risk assessments of BPA have been conducted by regulatory authorities as well as expert groups in Europe (SCF, 2002; ECB, 2003 and 2008; EFSA, 2006, 2008 and 2010), the United States (NTP-CERHR, 2008; US FDA, 2008; vom Saal *et al*., 2007), Canada (Health Canada, 2008) and Japan (AIST, 2005). In addition, an international expert meeting to assess the safety of BPA was recently organized by the World Health Organization (WHO) and the UN's Food and Agriculture Organization (FAO). An executive summary of conclusions from the meeting is available (FAO/WHO, 2010). Different methods for estimating exposure levels in the general population have been used in the different risk assessments of BPA (Table 1).

Calculations based on BPA concentrations in foods and environmental media combined with data on intake considered to be conservative for humans have most commonly been used in risk assessments to estimate daily intake of BPA. However, this approach has some weaknesses. Mainly, there is a lack of data on concentrations of BPA in different food products and environmental media, and also on food consumption in many cases, especially for children. This approach also assumes that the important sources of exposure have been identified, which may not be the case.

Calculations of total exposure to BPA have also been conducted based on BPA concentrations in biological samples. BPA is believed to be quickly metabolized in humans, the biological half-life is approximately 6 h, and is excreted in the urine in the form of BPA-glucuronide (Völkel *et al*., 2002). Consequently, urinary concentrations have often been considered to be an appropriate measurement of total BPA exposure (AIST, 2005; Lakind and Naiman, 2008 and 2010; NTP-CERHR, 2008). Calculations of exposure based on urinary concentrations generally result in lower estimated exposure levels than calculations based on food and environmental concentrations and intake. However, considering the short half-life of BPA, the timing of sampling may significantly influence measurements leading to both under- and overestimations of actual exposures.

In risk assessments of BPA exposure levels have generally been estimated around 0.07 – 14 µg/kg bw/day (Table 1). A much higher exposure estimate of 1500 µg/kg bw/day was derived in an assessment conducted by an expert group meeting at Chapel Hill, USA in 2006 (vom Saal *et al*., 2007; Vandenberg *et al*., 2007). The Chapel Hill experts based their estimation on reported human blood concentrations of BPA and physiology-based pharmacokinetic (PBPK) modelling and concluded that human exposure would have to greatly exceed 500 µg/kg bw/day in order

to account for the current human circulating levels of BPA. To further support this conclusion the Chapel Hill experts referred to the observations of Shin *et al*. (2004) who found in their rodent PBPK model that an oral intake of 100 mg BPA/day was needed to explain the mean human circulating level of 1.49 ng BPA/ml reported in a Japanese study (Takeuchi and Tsutsumi, 2002).

Most risk assessments of BPA have concluded that intake via food and drink is the main source of exposure of BPA in the general population. It has generally been concluded that, based on estimations derived from food consumption and concentration data, infants and/or young children have the highest BPA-exposure in the general population. This can be explained by a relatively high dietary intake via polycarbonate feeding bottles and tableware as well as canned foods. Children also consume a large amount of food per kg bw compared to adults. It should be pointed out that a high intake of canned food was often assumed, even for small children from 6 months old.

The conclusions that children seem to have a higher exposure to BPA (based on calculations of intake) are supported by studies where daily intake was estimated from urinary concentrations in the general population (Lakind and Naiman, 2008 and 2010; von Goetz *et al*., 2010)

It has recently been discussed that the reported levels of BPA in human urine and blood cannot be entirely explained by the calculated intake of BPA via food. Some possible explanations may be that human metabolism of BPA after oral exposure is not as efficient as previously believed and/or that other (unknown) sources of exposure contribute significantly to total exposure (Stalhut *et al*., 2009; Vandenberg *et al*., 2007).

3. Reported levels of BPA from potential sources of exposure

3.1 Exposure via food and drink

3.1.1 Baby bottles

Baby bottles made from polycarbonate are an important source of BPA exposure for infants (e.g. SCF, 2002; EFSA 2006; Health Canada, 2008, US FDA, 2008; von Goetz *et al*., 2010). Migration of BPA from bottles has been investigated in a number of published studies that have been summarized in Table 2.

Migration to water (commonly used as a simulant for milk or infant formula) under “normal use” conditions were typically in the range of 1-3 µg/l. However, it can be concluded that migration levels vary somewhat between studies. Variations in migration rates for BPA between brands were reported (Kubwabo *et al*., 2009) but it is also possible that the use of different

study conditions, i.e. incubation time and temperature, and methods for sample preparation and BPA analysis contribute to the variation in results.

Migration of BPA from the bottles increased with higher temperature (Kubwabo *et al*., 2009; Maragou *et al*., 2007) and longer incubation time (Kubwabo *et al*., 2009). However, there is no consistency between studies regarding if new or used bottles release more BPA.

3.1.2 Polycarbonate tableware

Information on migration levels from polycarbonate tableware, such as plastic mugs (e.g. trainer/"sippy" cups for small children), plates and cutlery, is not readily available in the published literature. Risk assessments of BPA have based estimations of BPA exposure from polycarbonate tableware on a few Japanese studies that seem not to be available in English (reviewed in e.g. AIST, 2005). The reported ranges of BPA migration from soup bowls, small dishes and deep dishes were 0.48-12.3 µg/bowl/meal, 0.14-0.78 µg/dish/meal and 0.18-39.4 µg/dish/meal, respectively in these studies (as described in AIST, 2005).

3.1.3 Food containers/microwave containers

Polycarbonate is commonly used in food storage and microwave containers, such as Tupperware, and in kitchen appliances. We were able to identify only one study, which investigated the potential migration of different compounds, including BPA, from polycarbonate containers intended for use in microwave ovens. In this study by Nerín *et al*. (2003) material from a polycarbonate container was dissolved in dichloromethane and analyzed using HPLC. Based on the concentration of BPA in the polycarbonate extract and assuming a contact surface of 6 dm^2, 1 kg of food and room temperature, the authors calculated the potential migration of BPA to food to be 6.5 µg/g food. As this was approximately double the specific migration limit established in the EU the containers under study were withdrawn from the market by the producer.

3.1.4 Polycarbonate drinking/water bottles

It has been shown that mean human urinary concentrations of BPA increased by 69% after drinking from reusable polycarbonate bottles during one week (Carwile *et al*. 2009). It seems reasonable to believe that migration from polycarbonate drinking bottles is similar to that from baby bottles. However, a few studies have especially investigated the migration of BPA from this type of bottle. These studies have been summarized in Table 3 and are also described below.

Cao and Corriveau (2008) tested BPA migration from two new bottles. The bottles were filled with boiling water and left at room temperature for 24 h. BPA concentrations in water samples were analyzed with GC-MS. BPA migration from the two bottles after 24 h were 1.7 and 4.1 µg/l.

Le *et al*. (2008) tested BPA migration from three new and five used bottles (it is not clear if they were the same brand). Bottles were filled with water and rotated on a cell culture roller bottle system at room temperature for up to 7 days. Samples were taken on days 1, 3, 5 and 7. In addition, two new and one used bottle were filled with boiling water and rotated at room temperature for 24 h at which time samples were taken. Three replicate experiments were conducted for each bottle. Samples were analyzed with ELISA. In this study BPA concentrations in water increased with time. However, migration from new and used bottles did not differ significantly. Concentrations ranged from 0.08 to 0.36 ng/ml on day 1 and from 0.34 to 1.33 on day 7. At seven days migration at room temperature averaged 0.6 and 0.42 ng/h for new and used bottles, respectively. Concentrations of BPA from heated water samples at 24 h ranged from 1.92 to 7.67 ng/ml, indicating that heated water greatly increased the migration of BPA from bottles in this study. Further, when the bottles that had been used for experiments with heated water were used again with water at room temperature BPA migration was still elevated compared to the initial experiments at room temperature, indicating a long-term effect on BPA release.

In a study by Kubwabo *et al*. (2009) five new bottles (it is not clear if they were the same brand) were tested for BPA migration to water for 2, 8, 24, 96 and 240 h at 40^{o}C and also for 24 h at 4^{o}C. In addition, ten used bottles (donated by staff at Health Canada) were tested for migration to water for 24 h at 40^{o}C and one used bottle for 24 h at 4^{o}C. Analyses were conducted using a GC-MS/MS method. The results were not very clearly reported, however, BPA migration from new bottles were found to increase with time and at 40^{o}C average concentrations ranged from 0.01 to 2.16 µg/l in tests conducted for 2-240 h. A significant difference in migration between new and used bottles was observed; after 24 h at 40^{o}C BPA concentrations were 0.01 and 0.20 µg/l in new and used bottles, respectively. Migration at 4^{o}C was lower than at 40^{o}C for both new and used bottles.

3.1.5 Canned food products and beverages

An important source of BPA exposure for adults and children seems to be the protective epoxy lining inside some food and beverage cans (AFFSA, 2010; von Goetz *et al*., 2010). Studies investigating BPA concentrations in canned food and beverages have been summarized in Tables 4 and 5, respectively. Reported levels of BPA show significant variations depending on type of food and also vary between studies for the same type of product.

Canned soups and sauces generally seem to contain the highest levels of BPA. Some studies also reported high levels of BPA in tuna fish (Table 4).

BPA has been detected in a wide variety of canned beverages but levels were in general lower than in canned food products (Table 5). The highest levels reported were from canned tea and coffee products investigated in one study (Lim *et al*., 2009). It has been discussed that BPA may

not always be detected in canned beverages due to the generally low levels of BPA in these products and the relatively high detection limits of analytical methods (Cao *et al*., 2009).

Storage time and temperature as well as different types of coating (organosol resin vs. epoxy resin) and damage to the cans do not seem to significantly influence the release of BPA from cans (Goodson *et al*., 2004; Munguia-Lopez *et al*., 2005). One study also included heating the food in the can but this treatment did not affect BPA migration (Goodson *et al*., 2004).

One study further investigated BPA concentrations in soft drinks and beer from glass and plastic bottles but could not detect any BPA in these products (Cao *et al*., 2010b). Hence, it seems that the main source of BPA found in canned beverages is from can coatings.

3.1.6 Canned infant formula

BPA has also been measured in canned infant feeding formula (Ackerman *et al*., 2010; Cao *et al*., 2008 and 2009b; Kuo and Ding, 2004). Levels of BPA in liquid infant formula ranged from 0.48 to 11 ng/g in two studies (Ackerman *et al*., 2010; Cao *et al*., 2008) while the levels of BPA in powdered formula reported in one study were 45-113 ng/g powder (Kuo and Ding, 2004). BPA concentrations in canned liquid formula were showed to increase after storage during 10 months at room temperature (Cao *et al*., 2009b).

Canned infant formula is not commonly available in Sweden, as far as we know. However, it is possible that formula and other food products intended for infants are packaged using other materials containing BPA (see section 3.1.7 below).

3.1.7 Food packaging

Apart from polycarbonate plastics and epoxy coatings of cans other materials in contact with food, such as food-contact papers and cardboards, may serve as potential sources of BPA exposure (Vandenberg *et al*., 2007; von Goetz *et al*., 2010). We identified two publications investigating the potential migration of BPA from paper and cardboard used in food applications. However, no studies measured the actual contamination of food items in contact with these materials.

Ozaki *et al*. (2004) measured BPA levels in 12 recycled and 16 virgin paper products in food contact use. These products included coffee filters, cooking paper, napkins, take-out wrapping paper and boxes, cake boxes and pizza boxes. The products were extracted with ethanol and analyzed by GC-MS. BPA was found in eight of 12 recycled products in concentrations ranging from 0.19-26 µg/g and in 13 of 16 virgin paper products at 0.034-0.36 µg/g.

Lopez-Espinosa *et al*. (2007) investigated the BPA contents in 40 paper and cardboard containers used for take-away food. The containers were collected from Belgium, Italy, Portugal

and Spain. Chemical residues were extracted from the inside of containers in contact with food. Analyses were conducted using HPLC and GC-MS. BPA was detected in 47% of the samples. Concentrations ranged from 0.05 to 1817 ng/g (geometric mean = 2.74 ng/g) in cardboard products and from 0.08 to 188 ng/g (geometric mean = 1.35 ng/g) in paper products.

3.1.8 Tap water

There is only limited information available for BPA concentrations in tap water. Three studies from China report levels ranging from 1 to 317 ng/l (Li *et al*., 2008; Li *et al*., 2010; Zhao *et al*., 2010). The potential sources of BPA in tap water were not discussed in these studies.

In Sweden measurements of BPA and BPA diglycidyl ether (BADGE) have been made in connection with relining of water pipes. Relining techniques include the use of polyester materials treated with epoxy, which is inserted into the pipe and heated to allow the material to polymerize *in situ*. If the epoxy does not polymerize completely BPA is free to leach into the water. In a pilot study conducted by Stockholm Vatten no BPA could be measured in water that had been left standing in a pipe for 72 hours after relining (Wahlberg *et al*., 2003). However, the limit of detection was 0.05 µg/l, indicating that the methods of analysis have to be improved in order to be able to quantify very low levels of BPA in tap water. BADGE was detected at levels around 1 µg/l in this study.

3.1.9 Breast milk

BPA has been found to be present in human breast milk in several studies from Japan, Korea and the USA (Kuruto-Niwa *et al*., 2007; Otaka *et al*, 2003; Sun *et al*., 2004; Ye *et al*., 2006 and 2008; Yi *et al*., 2010). These studies have been summarized in Table 6. Results vary significantly between studies and the highest concentrations reported were 87.7 ng/ml in a recent study by Yi *et al*. (2010). Concentrations in this study were about one order of magnitude higher than in previous studies but the reasons for these discrepancies were not discussed. In general, measured concentrations of BPA in breast milk were around 1-2 ng/ml. Different methods of sample preparation and analysis were used in different studies, which may account for some of the variations in results.

Yi *et al*. (2010) determined BPA concentrations in 100 breast milk samples from Korea using two different methods of analysis. Samples were analyzed using both HPLC with fluorescence detection and an LC-MS/MS method. Both methods showed similar LOD. However, concentrations measured with HPLC were more often below the LOD than those measured in the LC-MS/MS.

Interestingly, free, i.e. unconjugated, BPA was detected in breast milk in some studies (Ye *et al*., 2006 and 2008; Yi *et al*., 2010).

Risk assessments from the USA and Canada have estimated that maximum exposure to BPA via breast milk in infants is around 1 µg/kg bw/day (Health Canada, 2008; NTP-CERHR, 2008). At the recent FAO/ WHO expert meeting the mean and 95th percentile exposure to exclusively breast fed 0-6 months old infants was estimated to be 0.3 and 1.3 BPA µg/kg bw per day, respectively (FAO/WHO, 2010).

3.2 Toys

Information on the potential exposure to BPA from toys in children is extremely limited. One Japanese study investigated the migration of BPA from a variety toys (Fukuhara *et al*., 1999). Only a summary is available in English but this study was also summarized in the AIST risk assessment of BPA. Fragments of material were cut from toys and shaken in 100 ml water at 40^{o}C for 2 hours and samples were analyzed using hexane extraction followed by GC-MS. The maximum BPA level was 620 µg/l, observed with a plastic ball, which was not primarily intended to be placed in the mouth. All tested articles that were primarily intended to be placed in the mouth yielded BPA levels <37 µg/l.

A probabilistic exposure assessment of BPA in the Japanese population was conducted for the AIST risk assessment and has been published as a separate study (Miyamoto and Kotake, 2006). The average daily intake from toys for 0-5 and 6-11 month-old boys and was calculated to be 0.026 µg/kg bw and 0.069 µg/kg bw, respectively. These estimations were based on studies of daily mouthing time and migration of BPA from toys reported in Japanese literature (not available in English). The maximum migration of BPA from toys considered was 0.0162 µg/cm^2/min. Mouthing time of toys was 41.7±13.7 and 73.9±32.9 minutes per day for boys 0-5 and 6-11 months old, respectively. The area of the toy in contact with the mouth was assumed to be 10 cm^2.

3.3 Dental materials and other medical applications

Dental sealants and composite filling materials containing BPA are increasingly used in dentistry, especially in children (Fleisch *et al*., 2010). The most commonly used BPA-derived material is BPA glycidyl methacrylate (bis-GMA). BPA dimethacrylate (bis-DMA), BADGE and BPA ethoxylate dimethacrylate (bis-EMA) are also used. The resins are polymerized *in situ* during placement of dental sealants and unpolymerized material may be released into saliva directly after treatment. BPA may also be released over time due to hydrolysis of the resin caused by enzymatic activity of saliva, esterases, extreme pH and saliva storage (Pulgar *et al*, 2000; Schmalz *et al*., 1999). Risk assessments of BPA have so far generally concluded that exposure from dental materials does not contribute significantly to total exposure (AIST, 2005; ECB, 2003; EFSA, 2006; NTP-CERHR, 2008).

Several studies that have investigated the levels of BPA in saliva after the placement of dental sealants (e.g. Arenholt-Bindslev *et al* ., 1999; Fung *et al*., 2000; Joskow *et al*., 2006; Olea *et al*.,

1996), were recently reviewed by Fleisch *et al* (2010). There are large variations in results from these studies and also some scientific uncertainties due to methodological differences and limits of analytical detection.

A few studies have also investigated systemic absorption of BPA after placement of dental sealants. Two studies that measured levels in blood up to five days after sealant placement could not detect any BPA (Fung *et al*., 2000; Zimmerman-Downs, 2010). One other study found that median urinary levels of BPA increased from 2.4 ng/ml (pretreatment) to 12.9 ng/ml one hour after treatment with one type of sealant but treatment with another brand did not result in the same increase in urinary concentrations (Joskow *et al*., 2006). Urinary concentrations of BPA had decreased significantly by 24 h but were not completely back to baseline within this time.

Fleisch *et al*. (2010) concluded that BPA exposure after dental sealant placement is most likely an acute event. However, they discussed the possibility that the methods of analysis used in these studies may not be sensitive enough to detect very low levels of BPA.

BPA is also a component in other medical applications. It has been shown to migrate from hemodialyzers during simulated use with water and bovine serum (Haishima *et al*., 2000) and from cardiopulmonary bypass circuits during open heart surgery (Sakurai *et al*., 2002; *only an abstract is available in English*).

Calafat *et al*. (2008) investigated BPA exposure in 42 premature infants at two neonatal intensive care units. They found that mean concentrations of BPA in urine among premature infants undergoing intensive therapeutic medical interventions was 30.3 µg/l, which is one order of magnitude higher than among the general population. BPA was primarily found in its conjugated form, indicating that infants have some capacity to metabolize BPA.

3.4 Thermal printing paper

High levels of BPA in some types of cashier receipts were recently reported (Biedermann *et al*., 2010). The study showed that BPA was transferred from the paper to the skin by ”normal” handling of the receipts. Out of 13 thermal printing paper samples analyzed in this study 11 contained BPA, indicating that there are alternatives not containing BPA. BPA levels in the papers ranged from 8 to 17 g/kg. The amount of BPA transferred to the skin when taking hold of the paper with two fingers during approximately 5 seconds ranged from 0.2 to 6 µg. The transfer increased to about ten times more if fingers were wet or very greasy. Using different modes of holding the paper, e.g. low pressure, pulling paper through fingers, holding for longer time, did not affect the amount of BPA transferred to the skin. BPA transferred to skin by holding printing paper seemed to remain on the skin surface and could be washed off. However, when BPA was applied to the skin as a solution in ethanol it entered into the skin to such a depth that after 1 h no BPA was extractable, even using ethanol for up to 30 seconds.

Hence, the study did show that under certain conditions BPA can enter the skin to the extent where it is no longer possible to wash it off.

Dermal absorption of BPA is discussed in section 4, below.

3.5 Dust and air

BPA has been measured in dust and air samples in a few studies. These have been summarized in Table 7 and are also described below.

Matsumoto *et al*. (2005) measured BPA in urban ambient outdoor air during six months. Samples were collected using a high-volume air sampler situated on a roof top in Osaka, Japan and analyzed with GC-MS. BPA concentrations ranged from 0.02 to 1.92 ng/m^3, with a mean of 0.51 ng/m^3. Average concentrations varied somewhat between the months. The highest and lowest average concentrations were reported for February and October, respectively.

Wilson *et al*. (2007) investigated the potential sources of exposure to BPA and other phenols in 257 preschool children from North Carolina and Ohio. Samples of outdoor and indoor air and house dust, as well as soil, food and beverages, were collected from homes and daycare centers. Samples were analyzed with GC-MS. The LOD for the method was not clearly reported but can be presumed to be approximately 0.9 ng/m^3 in air and 20 ng/g in dust, based on the information given. Concentrations in indoor air from homes and daycare centers ranged from <LOD to 193 and 8.99 ng/m^3, respectively. Concentrations in outdoor air ranged from <LOD to 44.6 and 51.5 ng/m^3 in homes and daycare centers, respectively. Concentrations in dust ranged from <LOD to 707 and 156 ng/g in homes and daycare centers, respectively. It was concluded that about 99% of the exposure to BPA in preschool children were through the dietary ingestion route. Exposure from air and dust via inhalation was calculated to 14 and 7.8 ng/day in North Carolina and Ohio, respectively, corresponding to absorbed doses of 0.41 and 0.24 ng/kg bw/day, respectively (assuming 50% absorption).

Völkel *et al*. (2008) measured BPA in dust from 12 homes in Germany to investigate potential sources of contamination of urine samples in a biomonitoring study. Samples were collected by residents in homes using regular vacuum cleaners and analyzed with LC-MS/MS. BPA concentrations in dust ranged from 117 to 1486 µg/kg with a median of 553 µg/kg.

Geens *et al*. (2009) measured concentrations of BPA, as well as triclosan and TBBPA, in indoor dust from 18 homes and 2 offices in Belgium. Samples were collected using a vacuum cleaner and analyzed by LC-MS/MS. BPA concentrations measured in dust from homes ranged from 535 to 9729 ng/g with a mean and median of 2001 and 1461 ng/g, respectively. The concentrations of BPA in dust from the two offices were 4685 and 8380 ng/g. The reasons for the unusually high concentrations of BPA compared to earlier studies could not be entirely explained. Differences in sample collection and preparations between studies were discussed. However,

the measured levels of both triclosan and TBBPA were lower in this study than in previous studies. Despite the high levels of BPA in this study the authors concluded that intake from dust can be expected to contribute less than 5% to total BPA exposure in adults, assuming median concentrations of BPA.

Loganathan and Kannan (2011) measured BPA in dust from 50 homes and 6 laboratories in the Eastern U.S. Floor dust samples were obtained from vacuum cleaner bags and analyzed by HPLC-MS/MS. Four of the samples were collected from clothes-drier lint and two from the inside of refrigerators. Concentrations ranged from <LOD to 10200 ng/g with a mean and median of 843 and 422 ng/g, respectively. The highest concentration was measured in one of the laboratory samples. Concentrations in clothes-drier lint were in general lower than floor and refrigerator dust (range = <LOD – 34.8 ng/g, mean= 18.7 ng/g, median = 19.9 ng/g). The authors calculated that the median daily intake of BPA via dust for adults and toddlers were 0.35 and 5.63 ng/kg bw, respectively. The contribution of dust to total human intake of BPA was estimated to be <1%.

A recent Swedish study in 100 breast-feeding women found that women living in houses built after 1999 had significantly higher levels of BPA in blood compared to women living in older houses (Glynn *et al*. 2010). Concentrations of BPA in air and dust from homes were not analyzed in this study. However, the results indicate that newer homes could have higher indoor levels of BPA than older homes and that this is a factor influencing total human exposure to BPA.

4. Dermal absorption of BPA

Until recently exposure to BPA via the skin has not been considered to contribute significantly to total exposure. However, it has been discussed in recent reports that the levels of BPA measured in human urine and blood cannot be completely explained by the calculated levels of dietary intake (Vandenberg *et al*., 2007; Stahlhut *et al*., 2009). While one explanation may be that the kinetics of BPA may not be fully understood and that metabolism of BPA in humans is perhaps not as efficient as previously believed, it is also possible that other types of exposure, e.g. via the skin, contribute significantly to total exposure. However, there is only very limited information on the dermal absorption of BPA.

The ECB (2003) estimated that skin absorption of BPA is about 10% of the applied dose at 8 hours based on an unpublished *in vitro* study which used dermatomized human skin samples obtained from 3 donors. No reference was listed to identify the source.

Kaddar *et al*. (2008) found that dermal absorption of BPA was 14.9% in a study using pig skin. However, this study has several weaknesses, e.g. total recovery is low (84%) and the volume, area or thickness of the skin samples as well as receptor media used are not reported.

It should be noted that BPA is lipophilic (log K_{ow} = 3.4) and has a very low vapor pressure (5.3 x10-9 kPa at 25°C) and may therefore remain in the skin with potential for systemic uptake over time (Professor Gunnar Johanson, IMM, personal communication).

5. Prenatal exposure

Developmental toxicity has been especially implicated in the discussions concerning low-dose effects of BPA observed in animal studies (reviewed in Richter *et al*., 2007). Also, studies show that the human fetal liver has limited activity of glucuronidation (reviewed in Ring *et al*., 1999), the main metabolic pathway for BPA. The unborn child might thus be particularly sensitive to BPA toxicity.

Several studies in humans and experimental animals suggest that BPA can be transported across the placenta. However, there are a lot of uncertainties concerning the kinetics of BPA, for example with regard to species-differences, metabolism and half-life (particularly in fetuses and infants) as well as placental transport, making an estimate of exposure levels highly uncertain.

Measured BPA-concentrations in blood from pregnant women in human studies show considerable variations but the median and mean values are generally below 4 µg/L (Table 8). Because of the rapid metabolism of BPA, it may be difficult to estimate exposure from blood samples taken at a given moment. It should also be noted that it is not clear in several of these studies if free or total (free + conjugated) BPA was measured.

In most human studies BPA levels were lower in umbilical cord blood and in amniotic fluid than in maternal blood. Thus, it appears that the placenta may constitute some sort of biological barrier. However, there seems to be large uncertainties in terms of the kinetics of placental transfer and, to our knowledge, the mechanism of BPA-transport across the placenta is unknown.

There is some disagreement concerning the risks to the unborn child among risk assessments of BPA. EFSA has stated that BPA is efficiently metabolized in the pregnant woman and that the exposure of the fetus is negligible (EFSA 2008). However, given the large uncertainties that exist in regard to kinetics, exposure sources, routes of exposure and low-dose effects, it seems premature to assume that this is the case. Other risk assessments (e.g. Health Canada 2008 and NTP-CERHR 2008) have concluded that maternal exposure to BPA result in some concern for adverse effects in the fetus. So far no risk assessments have attempted to estimate prenatal exposure in the human population.

6. Conclusions

The aim of this report was primarily to review and summarize information from the open literature in order to identify and describe potential sources of exposure to BPA in the general population. It can be concluded that BPA has a very wide range of applications and therefore is present in many consumer products. It follows that there is a very large number of potential sources of BPA exposure. Some conclusions regarding which sources seem to be the most significant can be made. However, it is beyond the scope of this report to conduct a complete exposure assessment in order to quantify how much different sources potentially contribute to total BPA exposure. In addition, the lack of data, as well as diverging results, concerning concentrations of BPA in food, dust and air, and the migration of BPA from different materials undermine the reliability of such calculations. Comprehensive exposure assessments have previously been conducted for BPA (e.g. AIST, 2005; ECB, 2003 and 2008; NTP-CERHR, 2008; US FDA, 2008). However, these rely on different methods and assumptions and lack of data is often stated as a source of uncertainty in the calculations.

An investigation of potential sources of exposure to BPA in the general population was recently published (Von Goetz *et al*., 2010). The contribution to total BPA exposure from different food products, food-contact materials, house dust, air and dental sealants was estimated in this study. However, it was assumed that dermal exposure to BPA is negligible and that route of exposure was not considered in the calculations. In the study by von Goetz *et al*. (2010) the calculated aggregated daily exposure compares well with the calculations based on urinary concentrations for adults. However, their calculations of aggregated daily exposure for children (3-11 years old) generate daily exposure levels that are considerably lower (by a factor of two) compared to calculations based on urinary concentrations for this age group. This could indicate that important exposure routes may be lacking from their model of total exposure or that the pharmacokinetic model applied to urinary data overestimates exposure in children.

It has generally been concluded that exposure to BPA in the general population mainly occurs through intake of food and drink products that have been in contact with BPA-containing materials, such as polycarbonate or epoxy (e.g. AFFSA, 2010; AIST, 2005; ECB, 2003 and 2008; EFSA, 2006; Health Canada, 2008; NTP-CERHR, 2008; US FDA, 2008; Wilson *et al*., 2007). Exposure estimates based on calculations of intake from food and environmental media as well as estimates based on urinary concentrations of BPA measured in the human population indicate that children have a higher exposure to BPA per kg bw than adults (AFFSA, 2010; AIST, 2005; ECB, 2003 and 2008; EFSA, 2006; Health Canada, 2008; Lakind and Naiman, 2008 and 2010; NTP-CERHR, 2008; US FDA, 2008; von Goetz *et al.,* 2010).

Based on the information available in the open literature, as well as calculations conducted in various risk assessments of BPA, it is reasonable to believe that polycarbonate feeding bottles constitute the main source of BPA exposure for infants. Especially for infants that are fed exclusively from polycarbonate bottles until about six months of age. Several published studies

show that BPA migrates from polycarbonate feeding bottles at detectable levels (Table 2). Polycarbonate bottles and training (or "sippy") cups may also contribute significantly to total exposure in infants 6 – 12 months and older children. No studies specifically measuring the migration of BPA from polycarbonate training cups seem to be available but migration should be comparable to that of polycarbonate bottles. Migration from polycarbonate bottles was generally found to increase with higher temperatures. However, conclusions from studies vary in regard to if migration of BPA is higher from newer or older bottles or if there is any significant difference at all.

Canned food and beverages seem to be the most significant source of exposure to BPA for children older than 6 months, as well as for adults. These products contribute the most to total exposure in the general population in many exposure assessments conducted for BPA (AFSSA, 2010; ECB, 2003; EFSA, 2006; NTP-CERHR, 2008; von Goetz *et al.,* 2010). Very high concentrations of BPA were observed in some canned food products (Table 4) while levels in canned beverages generally were lower (Table 5). However, concentrations of BPA in canned products vary significantly between products and also between studies for the same type of product. This variability makes it difficult to estimate intake of BPA from this source and to what extent different canned products contribute to total exposure. It also has to be considered that there are differences in what canned products are typically consumed in different countries and estimates of exposure from this source from one part of the world may not be applicable in other areas. To our knowledge there are currently no data available on BPA concentrations in canned products on the Swedish market.

It seems that risk assessments of BPA often assume a high intake of canned food products and beverages even for infants in the age group 6 – 12 months (ECB, 2003; EFSA, 2006; NTP-CERHR, 2008). It is not clear whether this is because canned baby food is available in some countries or if there is an assumed intake of regular canned food in this age group. In any case, it is uncertain how well this reflects the situation in Sweden where baby food is packaged in glass jars. We found no information on BPA concentrations in baby food from glass jars. However, it seems possible that the metal lids of baby food jars are coated with epoxy and that this could be a source of BPA exposure.

Canned infant formula has also been reported to contribute significantly to total exposure in intake calculations for infants. To our knowledge canned infant formula is not commonly available in Sweden. However, infant formula as well as other food products intended for infants and small children is packaged using other materials that could contain and leach BPA, such as food-contact papers and cardboards. No information is available regarding the actual contamination of food items in contact with these materials.

It has been shown in one study that continuous use of reusable polycarbonate drinking bottles during one week increased the urinary levels of BPA by 69% in human volunteers (Carwile *et al*., 2009). However, we have no information on the use of such bottles in the Swedish population.

Very limited data is available concerning the migration of BPA from polycarbonate tableware and microwave containers. It is not possible to draw any reliable conclusions regarding the contribution from these sources to total BPA exposure.

There is not enough data to conclude whether tap water constitutes a significant source of exposure to BPA. In a few studies investigating BPA levels in tap water conducted in China concentrations ranged from 1 to 317 ng/l (Li *et al*., 2008; Li *et al*., 2010; Zhao *et al*., 2010). These studies do not discuss the possible sources of BPA in tap water. It is our understanding that relining of water pipes using materials containing epoxy would be the main source of BPA in tap water in Sweden but measurements taken after one relining event could not detect any BPA (Wahlberg *et al*., 2003). However, this may be due to insufficient sensitivity of analytical methods.

BPA has also been found in human breast milk. However, reported concentrations vary significantly between studies. The reasons for these differences are unclear but may in part be explained by differences in the analytical methods used. Risk assessments from the USA and Canada have estimated that maximum exposure to BPA via breast milk in infants is around 1 µg/kg bw/day (Health Canada, 2008; NTP-CERHR, 2008).

Data on migration of BPA from toys is very limited and seems only to be available in the Japanese literature. Average daily exposure to BPA from toys in Japanese male infants was estimated to be 0.026 µg/kg and 0.069 µg/kg for 0-5 and 6-11 month-old boys, respectively.

High levels of BPA in dust and air have been reported in some studies (Table 7). Measured concentrations varied greatly between studies, which may be a result of differences in the sampling techniques and analytical methods used. However, it is also possible that these results reflect “true” variations in BPA concentrations in air and dust. One Swedish study found that women living in houses built after 1999 had significantly higher urinary concentrations of BPA than women living in older houses (Glynn *et al*., 2010). While BPA concentrations in indoor air and dust were not measured in this study it is possible that BPA levels are higher in newly built houses due to the release unpolymerized BPA from new building materials, floors and furniture.

BPA has been found in high concentrations in thermal printing paper of receipts (Biedermann *et al*., 2010). The use and handling of thermal printing papers, such as certain receipts, may thus potentially contribute to total BPA exposure. However, it seems that normal handling of receipts results in transfer to the skin that can be washed off to a large extent. Still, exposure may occur if BPA is transferred to the fingers before handling food or eating, or if fingers are put in the mouth. It also seems that BPA can more easily be absorbed into the skin under certain circumstances. Also, if the skin is damaged higher absorption would be expected. However, little is known about dermal absorption of BPA and systemic uptake via the skin.

Polycarbonate is reportedly used in medical equipment, such as dialyzers, blood oxygenators and operating instruments (Plastics Europe, 2007), but there is very limited data on potential exposure to BPA from such applications of use. However, Calafat *et al*. (2008) found that

premature infants being treated in neonatal intensive care units had urinary levels of BPA that were about ten times higher than those of the general population. This is especially worrying as it implies a relatively high exposure in individuals that are particularly sensitive to the toxicity of BPA. Perinatal exposure to low levels of BPA in animal studies have been associated with effects on the development of reproductive organs and function as well as learning, memory and behavior (reviewed in Richter *et al*., 2007).

The reported migration of BPA from hemodialyzers may constitute an important source of exposure for patients with renal failure who would be continuously exposed during repeated treatments. In contrast, it is reasonable to believe that exposure to BPA from equipment used during surgeries, such as cardiopulmonary bypass circuits and operating instruments, do not contribute significantly to total BPA exposure since these applications most likely represent single, isolated events of exposure. Similarly, it seems that BPA exposure from materials used in dentistry is probably an acute, transient exposure in connection with placement of dental sealants. However, even though isolated single events of exposure to BPA may be assumed not to add significantly to total exposure in the general population they may still constitute important exposure scenarios for certain population groups. For example, one has to consider that if exposure of pregnant women occurs during sensitive windows of development it could potentially result in adverse effects in the fetus.

Several studies have commented on limitations in different analytical methods for measuring BPA in urine and blood (Fleisch *et al*., 2010; Völkel *et al*, 2005) as well as in environmental media (Wahlberg *et al*., 2003) and food products (Cao *et al*., 2009), e.g. relatively high LODs compared to the low levels of BPA expected. LC-MS/MS methods have been concluded to have sufficient sensitivity and higher power of separation compared to other techniques, e.g. HPLC with fluorescence detection, for quantifying BPA in blood and urine (Völkel *et al*., 2005) as well as in breast milk (Yi *et al*., 2010).

Contamination of samples has been discussed as a factor influencing the reliability of measurements of BPA in human tissues and in environmental samples (Völkel *et al*. 2005 and 2008). Contamination of samples from air and dust is a possibility. BPA may also be released from sampling devices, labware and reagents during sample collection and analysis.

There is sufficient human data to suggest that BPA is transferred across the placenta to the unborn child. However, there are considerable uncertainties concerning the kinetics of BPA, for example with regard to species-differences, metabolism and half-life (particularly in fetuses and infants) and transport across the placenta, making an estimate of exposure levels in the fetus highly uncertain.

In conclusion, based on the information available in the published literature as well as exposure assessments that have been made for BPA, polycarbonate baby feeding bottles and canned food and beverages seem to be the most significant sources of total human exposure to BPA in the general population. However, there is a lack of data concerning other potential sources of

exposure, especially regarding products on the Swedish market, as well as habits of Swedish consumers in regard to BPA-containing products, making it difficult to draw any definite conclusions regarding the most important exposure scenarios for the Swedish general population.

7. Data gaps and research needs

Considering that infants and young children seem to have the highest exposure to BPA the most important data gaps concern the identification and quantification of exposure from different sources in that group of the population.

- There is a lack of data with regard to concentrations in food products on the Swedish market. With the large variations observed in canned foods and beverages from other countries it would be useful to study the occurrence of BPA in these products in Sweden. It would also be important to investigate the pattern of consumption of these products in Sweden, i.e. what type of canned products are most commonly consumed, compared to other countries for which exposure assessments and calculations of intake are available.
- In terms of infants between 6 and 12 months we consider it unlikely that intake of canned food products is as common in Sweden as has been assumed in risk assessments from other countries. We have found no information on BPA concentrations in baby food packaged in glass jars. We assume that metal lids of such jars may be coated with epoxy and this, as well as any migration of BPA from such coatings, should be investigated further.
- Canned infant formula is, to our knowledge, not commonly sold in Sweden. However, infant formula and other food products intended for infants are packaged using other materials, such as food-contact papers and cardboards. These materials have been shown to contain BPA but actual contamination of food items in contact with them has not been studied. In order to be able to make a comprehensive evaluation of exposure to infants (and other population groups) via different food products migration of BPA from these materials need to be further investigated.
- There is a lack of data on the migration of BPA to food (other than water used as a simulant for milk and infant formula) heated in polycarbonate containers in microwave ovens. Further studies are needed in order to estimate exposure during such scenarios.
- Data on exposure to BPA from toys is extremely limited. Further studies investigating the potential migration of BPA from toys are needed in order to enable estimations of exposure to children from this source.
- Information is very limited in regard to skin absorption of BPA. This needs to be further studied in order to assess the potential dermal exposure of BPA, e.g. from handling cashiers receipts.

- Indoor air and dust is a potential source of exposure to BPA. However, there are large variations in data and it is unclear whether these variations reflect “true” variations of BPA in these media or if they are due to differences in sampling techniques and/or insufficient analytical methods. Further measurements are needed to verify existing data and also to investigate levels in air and dust in Sweden.

8. References

Ackerman LK, Noonan GO, Heiserman WM, Roach JA, Limm W, Begley TH. 2010. Determination of bisphenol A in U.S. infant formulas: updated methods and concentrations. J Agric Food Chem 24: 2307-2313.

AFSSA – The French Food Agency. 2010. Opinion of the French Food Agency regarding exposure to bisphenol A in the French population and maximum levels of bisphenol A in foods. Available on-line at www.afssa.fr

AIST – Japanese National Institute of Advanced Industrial Science and Technology. 2005. Risk Assessment Document Series No 4: Bisphenol A. Available on-line at: www.aist.go.jp

Beronius A, Rudén C, Håkansson H, Hanberg A. 2010. Risk to all or none? A comparative analysis of controversies in the health risk assessment of Bisphenol A. Reprod Toxicol 29(2): 132-146.

Biedermann S, Tschudin P, Grob K. 2010. Transfer of bisphenol A from thermal printer paper to the skin. Anal Bioanal Chem 398: 571-576.

Biedermann-Brem S, Grob K, Fjeldal P. 2008. Release of bisphenol A from polycarbonate baby bottles: mechanisms of formation and investigation of worst case scenarios. Eur Food Res Technol 227:1053–1060.

Braunrath R, Podlipna D, Padlesak S, Cichna-Markl M. 2005. Determination of bisphenol A in canned foods by immunoaffinity chromatography, HPLC, and fluorescence detection. J Agric Food Chem 53: 8911-8917.

Brede C, Fjeldal P, Skjevrak I, Herikstad H. 2003. Increased migration levels of bisphenol A from polycarbonate baby bottles after dishwashing, boiling and brushing. Food Addit Contam 20: 684-689.

Calafat AM, Weuve J, Ye X, Jia LT, Hu H, Ringer S, *et al*. 2009. Exposure to bisphenol A and other phenols in neonatal intensive care unit premature infants. Environ Health Perspect 117: 639-644.

Calafat AM, Ye X, Wong L-Y, Reidy JA, Needham LL. 2008. Exposure of the U.S. population to bisphenol A and 4-*tertiary*-octylphenol: 2003-2004. Environ Health Perspect 116: 39-44.

Cao X-L, Corriveau J, Popovic S. 2009a. Levels of bisphenol A in canned soft drink products in Canadian markets. J Agric Food Chem 57: 1307-1311.

Cao X-L, Corriveau J, Popovic S. 2009b. Migration of bisphenol A from can coatings to liquid infant formula during storage at room temperature. J Food Prot 72: 2571-2574.

Cao X-L, Corriveau J, Popovic S. 2010a. Bisphenol A in canned food products from Canadian markets. J Food Prot 73: 1085-1089.

Cao X-L, Corriveau J, Popovic S. 2010b. Sources of low concentrations of bisphenol A in canned beverage products. J Food Prot 73: 1548-1551.

Cao X-L, Corriveau J. 2008. Determination of bisphenol A in water by isotope dilution headspace solid-phase microextraction and gas chromatography/mass spectrometry without derivatization. J AOAC 91: 622-628.

Cao X-L, Dufresne G, Belisle S, Clement G, Falicki M, Beraldin F *et al*. 2008. Levels of bisphenol A in canned liquid infant formula products in Canada and dietary intake estimates. J Agric Food Chem 56: 7919-7924.

Carwile JL, Luu HT, Bassett LS, Driscoll DA, Yuan C, Chang JY, *et al*. 2009. Use of Polycarbonate Bottles and Urinary Bisphenol A Concentrations. Environ Health Perspect 117: 1368-1372.

ECB – European Chemicals Bureau. 2003. European Union risk assessment report: 4,4'-isopropylidenediphenol (Bisphenol-A). Available on-line at: http://ecb.jrc.ec.europa.eu/

ECB – European Chemicals Bureau. 2008. Updated risk assessment of 4,4'-isopropylidenediphenol (Bisphenol-A). Available on-line at: http://ecb.jrc.ec.europa.eu/

EFSA – European Food Safety Authority. 2006. Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food on a request from the Commission related to 2,2-bis(4-hydroxyphenyl)propane (bisphenol A). Available on-line at: www.efsa.europa.eu

EFSA – European Food Safety Authority. 2008. Toxicokinetics of Bisphenol A. Scientific Opinion of the Panel on Food additives, Flavourings, Processing aids and Materials in Contact with Food (AFC). Available on-line at: www.efsa.europa.eu

Ehlert KA, Beumer CWE, Groot, MCE. 2008. Migration of bisphenol A into water from polycarbonate baby bottles during microwave heating. Food Addit Contam 25: 904-910.

FAO/WHO. 2010. Summary report from the joint FAO/WHO expert meeting to review toxicological and health aspects of bisphenol A. available on-line at www.who.int.

Fleisch AF, Sheffield PE, Chinn C, Edelstein BL, Landrigan PJ. 2010. Bisphenol A and related compounds in dental materials. Pediatrics 126:760-8.

Fung EY, Ewoldsen NO, St Germain HA Jr, Marx DB, Miaw CL, Siew C *et al*. 2000. Pharmacokinetics of bisphenol A released from a dental sealant. J Am Dent Assoc 131: 51-58.

Geens T, Apelbaum TZ, Goeyens L, Neels H, Covaci A. 2010. Intake of bisphenol A from canned beverages and foods on the Belgian market. Food Addit Contam 27: 1627-1637.

Glynn A, Lignell S, Danerud PO, Aune M, Törnkvis A, Ankarberg E *et al*. 2010. Sakrapport till Naturvårdsverkets Miljöövervakning: Nonylfenol och bisphenol A i blod från ammande kvinnor

från Uppsalatrakten. Available on-line at:
www.imm.ki.se/Datavard/Rapporter/Sakrapport.pdf (in Swedish).

Goodson A, Robin H, Summerfield W, Cooper I. 2004. Migration of bisphenol A from can coatings-effects of damage, storage conditions and heating. Food Addit Contam 21: 1015-1026.

Goodson A, Summerfield W, Cooper I. 2002. Survey of bisphenol A and bisphenol F in canned foods. Food Addit Contam 19: 796-802.

Grumetto L, Montesano D, Seccia S, Albrizio S, Barbato F. 2008. Determination of bisphenol A and bisphenol B residues in canned peeled tomatoes by reversed-phase liquid chromatography. J Agric Food Chem 56: 10633-10637.

Haishima Y, Hayashi Y, Yagami T, Nakamura A. 2001. Elution of bisphenol-A from hemodialyzers consisting of polycarbonate and polysulfone resins. J Biomed Mater Res 58: 209-215.

Health Canada. 2008. Screening assessment for the Challenge Phenol, 4,4'-(1-methylethylidene)bis- (Bisphenol A). Available on-line at: www.hc-sc.gc.ca

Ikezuki Y, Tsutsumi O, Takai Y, Kamei Y, Taketani Y. 2002. Determination of bisphenol A concentrations in human biological fluids reveals significant early prenatal exposure. Hum Reprod 17: 2839-2841.

Joskow R, Barr DB, Barr JR, Calafat AM, Needham LL, Rubin C. 2006. Exposure to bisphenol A from bis-glycidyl dimethacrylate-based dental sealants. J Am Dent Assoc 137:353-362.

Kaddar N, Harthé C, Déchaud H, Mappus E, Pugeat M. 2008. Cutaneous penetration of bisphenol A in pig skin. J Toxicol Environ Health A 71: 471-473.

Kubwabo C, Kosarac I, Stewart B, Gauthier BR, Lalonde K, Lalonde PJ. 2009. Migration of bisphenol A from plastic baby bottles, baby bottle liners and reusable polycarbonate drinking bottles. Food Addit Contam 26: 928-937.

Kuo HW, Ding WH. 2004. Trace determination of bisphenol A and phytoestrogens in infant formula powders by gas chromatography-mass spectrometry. J Chromatogr A 1027: 67-74.

Kuruto-Niwa R, Tateoka Y, Usuki Y, Nozawa R. 2007. Measurement of bisphenol A concentrations in human colostrum. Chemosphere 66: 1160-1164.

LaKind JS, Naiman DQ. 2008. Bisphenol A (BPA) daily intakes in the United States: Estimates from the 2003-2004 NHANES urinary BPA data. J Expo Sci Environ Epidemiol 18: 608-615.

Lakind JS, Naiman DQ. 2010. Daily intake of bisphenol A and potential sources of exposure: 2005-2006 National Health and Nutrition Examination Survey. J Expo Sci Environ Epidemiol *Epub ahead of print*. DOI: 10.1038/jes.2010.9

Le HH, Carlson EM, Chua JP, Belcher SM. 2008. Bisphenol A is released from polycarbonate drinking bottles and mimics the neurotoxic actions of estrogen in developing cerebellar neurons. Toxicol Lett 176: 149-156.

Lee YJ, Ryu HY, Kim HK, Min CS, Lee JH, Kim E, et al. 2008. Maternal and fetal exposure to bisphenol A in Korea. Reprod Toxicol 25: 413-419.

Li X, Ying G-G, Su H-C, Ying X-B, Wang L. 2010. Simultaneous determination and assessment of 4-nonylphenol, bisphenol A and triclosan in tap water, bottled water and baby bottles. Environment International 36: 557-562.

Lim DS, Kwack SJ, Kim K-B, Kim HS, Lee BM. 2009. Risk assessment of bisphenol A migrated from canned foods in Korea. J Toxicol Environ Health A 72: 1327-1335.

Loganathan SN, Kannan K. 2011. Occurrence of Bisphenol A in Indoor Dust from Two Locations in the Eastern United States and Implications for Human Exposures. Arch Environ Contam Toxicol *Epub ahead of print.*

Lopez-Espinosa MJ, Granada A, Araque P, Molina-Molina JM, Puertollano MC, Rivas A *et al*. 2007. Oestrogenicity of paper and cardboard extracts used as food containers. Food Addit Contam 24: 95-102.

Maragou NC, Makri A, Lampi EN, Thomaidis NS, Koupparis MA. 2008. Migration of bisphenol A from polycarbonate baby bottles under real use conditions. Food Addit Contam 25: 373-383.

Miyamoto K, Kotake M. 2006. Estimation of daily bisphenol A intake of Japanese individuals with emphasis on uncertainty and variability. Environ Sci 13: 15-29.

Mountfort KA, Kelly J, Jickells SM, Castle L. 1997. Investigations into the potential degradation of polycarbonate baby bottles during sterilization with consequent release of bisphenol A. Food Addit Contam 14: 737-740.

Munguía-López EM, Gerardo-Lugo S, Peralta E, Bolumen S, Soto-Valdez H. 2005. Migration of bisphenol A (BPA) from can coatings into fatty-food simulant and tuna fish. Food Addit Contam 22: 892-898.

Nerín C, Fernández C, Domeno C, Salafranca J. 2003. Determinatino of potential migrants in polycarbonate containers used for microwave ovens by high-performance liquid chromatography with ultraviolet and fluorescence detection. J Agric Food Chem 51: 5647-5653.

NTP-CERHR – National Toxicology Program Center for the Evaluation of Risks to Human Reproduction. 2008. Monograph on the potential human reproductive and developmental effects of bisphenol A. Available on-line at: http://cerhr.niehs.nih.gov/

Otaka H, Yasuhara A, Morita M. 2003. Determination of bisphenol A and 4-nonylphenol in human milk using alkaline digestion and cleanup by solid-phase extraction. Anal Sci 19: 1663-1666.

Ozaki A, Yamaguchi Y, Fujita T, Kuroda K, Endo G. 2004. Chemical analysis and genotoxicological safety assessment of paper and paperboard used for food packaging. Food Chem Toxicol 42: 1323-1337.

Pérez-Bendito MD, Rubio-Bravo S, Lunar-Reyes ML García-Prieto A. 2009. Determination of bisphenol A in canned fatty foods by coacervative microextraction, liquid chromatography and fluorimetry. Food Addit Contam 26: 265-274.

Plastics Europe. 2007. Applications of bisphenol A. Available on-line at www.bisphenol-a-europe.org

Rastakari N, Ahmadkhaniha R, Yunesian M, Baleh LJ, Mesdaghinia A. 2010. Sensitive determination of bisphenol A and bisphenol F in canned food using solid-phase microextraction fibre coated with single-walled carbon nanotubes before GC/MS. Food Addit Contam 27: 1460-1468.

Richter CA, Birnbaum LS, Farabollini F, Newbold RR, Rubin BS, Talsness CE, et al. 2007. *In vivo* effects of bisphenol A in laboratory rodent studies. Reprod Toxicol 24: 199-224.

Ring JA, Ghabrial H, Ching MS, Smallwood RA, Morgan DJ. 1999. Fetal hepatic drug elimination. Pharmacol Ther 84: 429-445.

Sajiki J, Miyamoto F, Fukata H, Mori C, Yonekubo J, Hayakawa K. 2007. Bisphenol A (BPA) and its source in foods in Japanese markets. Food Addit Contam 24: 103-112.

Sakurai h, Maeda M, Miyahara K, Nakayama M, Murayama H, Hasegawa H *et al*. 2002. Extraction of bisphenol-A from a cardiopulmonary bypass circuit. *(Only abstract available in English)* Kyobu Geka 55: 770-772.

SCF – Scientific Committee on Food of the European Commission - Health & Consumer Protection Directorate-General. 2002. Opinion of the Scientific Committee on Food on Bisphenol A. Available on-line at: http://ec.europa.eu/food/index_en.htm

Schmalz G, Preiss A, Arenholt-Bindslev D. 1999. Bisphenol-A content of resin monomers and related degradation products. Clin Oral Investig 3: 114-119.

Schönfelder G, Wittfoht W, Hopp H, Talsness CE, Paul M, Chahoud I. 2002. Parent bisphenol A accumulation in the human maternal-fetal-placental unit. Environ Health Perspect 110: A703-A707.

Shin BS, Kim CH, Jun YS, Kim DH, Lee BM, Yoon CH, *et al*. 2004. Physiologically based pharmacokinetics of bisphenol A. J Toxicol Environ Health A 67:1971-85.

Stahlhut RW, Welshons WV, Swan SH. 2009. Bisphenol A data in NHANES suggest longer than expected half-life, substantial nonfood exposure, or both. Environ Health Perspect 117:784-9.

Sun Y, Irie M, Kishikawa N, Wada M, Kuroda N, Nakashima K. 2004. Determination of bisphenol A in human breast milk by HPLC with column-switching and fluorescence detection. Biomed Chromatogr 18(8): 501-507.

Sun Y, Wada M, Al-Dirbashi O, Kuroda N, Nakazawa H, Nakashima K. 2000. High-performance liquid chromatography with peroxyoxalate chemiluminescence detection of bisphenol A migrated from polycarbonate baby bottles using 4-(4,5-diphenyl-1Himidazol-2-yl)benzoyl chloride as a label. J Chromatogr B 74: 49-56.

Takeuchi T, Tsutsumi O. 2002. Serum bisphenol A concentrations showed gender differences, possibly linked to androgen levels. Biochem Biophys Res Commun 291:76-8.

Thomson BM, Grounds PR. 2005. Bisphenol A in canned foods in New Zealand: an exposure assessment. Food Addit Contam 22: 65-72.

Tyl RW, Myers CB, Marr MC, Sloan CS, Castillo NP, Veselica MM, et al. 2008. Two-generation reproductive toxicity study of dietary bisphenol A in CD-1 (Swiss) mice. Toxicol Sci 104: 362-384.

Tyl RW, Myers CB, Marr MC, Thomas BF, Keimowitz AR, Brine DR, et al. 2002. Three-generation reproductive toxicity study of dietary bisphenol A in CD sprague-Dawley rats. Toxicol Sci 68: 121-146.

US Food and Drug Administration (FDA). 2008. Draft assessment of bisphenol A for use in food contact applications. Available on-line at: www.fda.gov

Vandenberg LN, Hauser R, Marcus M, Olea N, Welshons WV. 2007. Human exposure to bisphenol A (BPA). Reprod Toxicol 24:139-77.

Völkel W, Bittner N, Dekant W. 2005. Quantitation of bisphenol A and bisphenol A glucuronide in biological samples by high performance liquid chromatography-tandem mass spectrometry. Drug Metab Dispos 33(11): 1748-1757.

Völkel W, Colnot T, Csanady GA, Filser JG, Dekant W. 2002. Metabolism and kinetics of bisphenol A in humans at low doses following oral administration. Chem Res Toxicol 15(10): 1281-1287.

Völkel W, Kiranoglu M, Fromme H. 2008. Determination of free and total bisphenol A in human urine to assess daily uptake as a basis for a valid risk assessment. Toxicol Lett 179(3): 155-162.

vom Saal FS, Belcher SM, Guillette LJ, Hauser R, Myers JP. 2007. Chapel Hill bisphenol A expert panel consensus statement: integration of mechanisms, effects in animals and potential to impact human health at current levels of exposure. Reprod Toxicol 24:131-8.

von Goetz N, Wormuth M, Scheringer M, Hungerbuhler K. 2010. Bisphenol a: how the most relevant exposure sources contribute to total consumer exposure. Risk Anal 30:473-487.

Wahlberg C, Berg C, Melin B. 2003. Inverkan på dricksvattenkvaliteten från strumpinfodring av Pålsundsledningen. Stockholm Vatten. Rapport nr 11-2003. Available on-line at http://www.stockholmvatten.se/commondata/rapporter/dricksvatten/Dricksvattenkvalitet/Inverkan_dricksv_strumpinf_Palsundsl.pdf (in Swedish).

Wilson NK, Chuang JC, Morgan MK, Lordo RA, Sheldon LS. 2007. An observational study of the potential exposures of preschool children to pentachlorophenol, bisphenol-A, and nonylphenol at home and daycare. Environ Res 103:9-20.

Yamada H, Furuta I, Kato EH, Kataoka S, Usuki Y, Kobashi G, et al. 2002. Maternal serum and amniotic fluid bisphenol A concentrations in the early second trimester. Reprod Toxicol 16: 735-739.

Ye X, Bishop AM, Needham LL, Calafat AM. 2008. Automated on-line column-switching HPLC-MS/MS method with peak focusing for measuring parabens, triclosan, and other environmental phenols in human milk. Anal Chim Acta 622: 150-156.

Ye X, Kuklenyik Z, Needham LL, Calafat AM. 2006. Measuring environmental phenols and chlorinated organic chemicals in breast milk using automated on-line column-switching – high performance liquid chromatography – isotope dilution tandem mass spectrometry. J Chromatogr B 831: 110-115.

Yi B, Kim C, Yang M. 2010. Biological monitoring of bisphenol A with HPLC/FLD and LC/MS/MS assays. J Chromatogr B. 878:2606-10.

Yonekubo J, Hayakawa K, Sajiki J. 2008. Concentrations of bisphenol A, bisphenol A diglycidyl ether, and their derivatives in canned foods in Japanese markets. J Agric Food Chem 56: 2041.2047.

Yoshida T, Horie M, Hoshino Y, Nakazawa H. 2001. Determination of bisphenol A in canned vegetables and fruit by high performance liquid chromatography. Food Addit Contam 18: 69-75.

Zimmerman-Downs JM, Shuman D, Stull SC, Ratzlaff RE. 2010. Bisphenol A blood and saliva levels prior to and after dental sealant placement in adults. J Dent Hyg 84: 145-150.

9. Tables

Table 1. Summary of exposure assessments for the general population from different risk assessments of BPA. The most highly exposed sub-groups as well as the highest exposure levels identified in each assessment are presented.

Risk assessment	Type of exposure considered	Most highly exposed per kg bw	Highest estimated exposure (µg/kg bw/day)	Basis for exposure estimates
SCF 2002	Oral, via diet	Formula fed infants 0-4 months old	1.6[a]	Based on realistic worst-case migration from polycarbonate bottles and highest intake
ECB 2003	Oral, via diet	Children 1.5-4.5 years old Adults	14[a] 9[a]	Based on realistic worst-case migration from food cans (100 µg/kg), beverage cans (10 µg/kg) and polycarbonate tableware and containers (5 µg/kg) and 97.5th percentile daily intake of canned food and beverage and wine.
	Environmental (contaminated fish, meat vegetables, water and air)	*Calculated for adults only*	0.018 (regional) [a], 60 (local, close to PVC production plant) [a]	Based on modeling using the EUSES software
AIST 2005	Aggregate (food and environment)	Children 1-6 years old[c]	4.1[a], 1.2[b]	Based on measured ranges of concentrations in food, and the environment (atmosphere, toys, etc) and ranges of intake from consumptions studies, pulmonary absorption, mouthing of toys, etc.
	Total	*Calculated for adults only*[c]	0.043 – 0.075 [a], 0.034 – 0.059 [b]	Based on urinary concentrations
EFSA 2006 and 2008	Oral, via diet	Formula fed infants 6 months old	13[a], 8.3[b]	Based on typical (average) and upper (worst case) value of BPA concentrations in formula respectively and highest consumption rates
vom Saal *et al*., 2007; Vandenberg *et al*., 2007 (**Chapel Hill 2007)**	Total	*Calculated for adults only*	1500[bd]	Based on reports of median human circulating levels and rodent PBPK models.
ECB 2008	Oral, via diet	Children 1.5-4.5 years old Adults	10[a] 1.5[a]	Based on realistic worst-case migration from food cans (50 µg/kg), beverage cans (10 µg/kg) and polycarbonate tableware and containers (5 µg/kg) and an assumed consumption of 2 and 3 kg food and beverages per day

				for children and adults, respectively.
	Environmental (contaminated fish, meat vegetables, water and air)	*Calculated for adults only*	0.009 (regional) [a], 41 (local, close to BPA production plant) [a]	Based on modeling using the EUSES software
Health Canada 2008	Oral, via diet	Formula fed infants	4.12[a]	Based on max concentrations of BPA measured in liquid formula, average migration from polycarbonate bottles to boiling water and max consumption
	Aggregate (food and environment)	Formula fed infants	4.30[a]	Based on max concentrations of BPA measured in liquid formula, average migration from polycarbonate bottles to boiling water and max intake, as well as max concentrations in environmental media
NTP-CERHR 2008	Oral, via diet	Children 1.5-4.5 years old	14.7[a]	Based on worst-case migration from food cans and an assumed consumption of 2 kg/day of canned food
	Total	Children 6-8 years old	2.17[a], 0.07[b]	Based on urinary metabolites in 90 US girls 6-8 years old, and assuming 100% urinary excretion of BPA in 24 hours
	Total	Teenagers 12-19 years old	0.077[b]	Based on urinary metabolites assuming 100% excretion of BPA in 24 hours
US FDA 2008	Oral, via diet	Formula fed infants 1-2 months old[c]	2.42[b]	Based on realistic worst case migration from polycarbonate bottles, average BPA concentration in liquid formula and mean intake
WHO 2010	Aggregate (food and environment)	Formula fed infants 0–6 months old	4.5[a], 2.4[b]	Based on concentrations of BPA measured in liquid formula (unclear if the range, average or max concentration was considered) and max migration from polycarbonate bottles to boiling water. Unclear how intake (i.e. ml of formula/day) was estimated.

[a] Estimated worst case exposure levels or 95th percentile

[b] Estimated average or "typical" exposure levels

[c] Different estimates for males and females. Female exposure levels were marginally higher and are therefore reported here for the sake of comparisons.

[d] Estimated exposure was given as 100 mg/adult/day and was adjusted assuming a body weight of 65 kg.

Table 2. Migration of BPA from polycarbonate baby feeding bottles reported in the published literature.

Study	Samples	Food (simulant)	Incubation temperature (°C)	Incubation time	Method of analysis	LOD (µg/l)	BPA migration (µg/l)	
							Range	Mean
Li *et al.*, 2010	12 new bottles of 4 different brands during "normal use" conditions	Milli-Q grade water	24	24h and 3, 5, 7 days	GC-MS	$7x10^{-4}$	24h: <LOD – 1.11[a] 3d: 0.008 – 0.35 5d: <LOD – 0.13 7d: <LOD – 0.21	--
	12 new bottles of 4 different brands during "normal use" conditions	Milli-Q grade water	40	24h and 3, 5, 7 days	GC-MS	$7x10^{-4}$	24h: 0.038 – 4.11 3d: 0.10 – 0.99 5d: 0.16 – 1.06 7d: 0.004 – 0.67	--
	12 new bottles of 4 different brands during high temperature conditions	Milli-Q grade water	Filled with boiling water and left at room temp	24h	GC-MS	$7x10^{-4}$	0.14 – 18.8	--
Kubwabo *et al.*, 2009	14 new bottles of different brands at "body temperature"	HPLC-grade water	40	8, 24 and 240h	GC-MS/MS	$4x10^{-5}$	--	8h: 0.11[b] 24h: 0.12 240h: 1.88
	14 new bottles of different brands at "body temperature"	50% ethanol/HPLC water	40	8, 24 and 240h	GC-MS/MS	$4x10^{-5}$	--	8h: 0.17 24h: 1.52 240h: 2.39
	14 new bottles of different brands at high-temperature	HPLC-grade water	60	24h	GC-MS/MS	$4x10^{-5}$	--	1.77
	9 new bottles of different brands after dishwashing	HPLC-grade water	40	2h	GC-MS/MS	$4x10^{-5}$	--	0.01[c]
Cao and Corriveau, 2008	3 new bottles	Water (purity not stated)	Filled with boiling water and left at room temp	24h	GC-MS	0.05	2.4-3.6	--
Ehlert *et al.*, 2008	18 new bottles of different brands sterilized for 5 min in boiling water and after 2 cycles of rinsing and drying ("normal use")	HPLC-grade water	Heated in microwave and allowed to boil for 1 min.	Not stated – cooled in water bath until temp reached 37°C	GC-MS	0.1	1st: <LOD-0.49[d] 2nd: <LOD-0.73 3rd: <LOD-0.30	--
Biedermann-Brem *et al.*, 2008	4 new bottles of different brands	Extraction by MTBE	Room temp?	1 min	HPLC-FL	0.01	0.16-0.38	--
	4 bottles of different brands after 30 cycles of washing	Extraction by MTBE	Room temp?	1 min	HPLC-FL	0.01	0.17-0.32	--

	1 bottle after simulated "harsh" washing cycle with 2% laboratory detergent	Water (purity not stated)	80	1h	HPLC-FL	0.01	690	--
	1 bottle after simulated "harsh" washing cycle with 5% laboratory detergent	Water (purity not stated)	80	1h	HPLC-FL	0.01	1580	--
	1 new bottle into solutions with different pH	Different solutions ranging from pH 2-12	80	1h	HPLC-FL	0.01	pH 2: 1.3 pH 6: 20 pH 8: 6 pH 9: 25 pH 11: 1640 pH 12: 1010	--
	1 "used" bottle into solutions with different pH	Different solutions ranging from pH 2-12	80	1h	HPLC-FL	0.01	pH 2: 2 pH 6: 12 pH 8: 3 pH 9: 9 pH 11: 570 pH 12: 350	--
Maragou *et al.*, 2007	3 new bottles each of 2 different brands after 10 cycles of dishwashing and sterilization	3% acetic acid	70	2h	HPLC-FLD	1.8	<LOD	--
	4 new bottles each of 2 different brands after 10 cycles of dishwashing and sterilization	HPLC-grade water	70	2h	HPLC-FLD	2.4	<LOD	--
	4 new bottles each of 2 different brands after 10 cycles of dishwashing and 10 cycles of brushing with detergent and sterilization	HPLC-grade water	70	2h	HPLC-FLD	2.4	<LOD	--
	4 new bottles each of 2 different brands ("old bottles") after 5 cycles of brushing with detergent and sterilization [e]	HPLC-grade water	Filled with boiling water and left at room temp	45 min	HPLC-FLD	2.4	--	<LOD – 14.3±0.4[f]
	14 new bottles of 4 different brands after 12 cycles of brushing with detergent and sterilization	HPLC-grade water	Filled with boiling water and left at room temp	45 min	HPLC-FLD	2.4	--	<LOD – 10.6±2.7[f]
Brede *et al.*, 2003	12 new bottles	Water (purity not stated)	Filled with hot water and kept in	1h	GC-MS	0.1	0.11-0.43	0.23±0.12

			100°C oven					
	12 bottles after 51 cycles in dishwasher and occasionally boiled or brushed	Water (purity not stated)	Filled with hot water and kept in 100°C oven	1h	GC-MS	0.1	3.7-17.7	8.4±4
	12 bottles after 169 cycles in dishwasher and occasionally boiled or brushed	Water (purity not stated)	Filled with hot water and kept in 100°C oven	1h	GC-MS	0.1	3.1-15.2	6.7±4
Sun *et al*., 2000	2 new bottles (4 runs/bottle), 1st use	Water (purity not stated)	Filled with boiling water and kept in 95°C oven	30 min	HPLC-PO-CL	0.38[g]	--	0.59±0.08 and 0.75±0.09[g]
	2 new bottles (4 runs/bottle), 2nd use	Water (purity not stated)	Filled with boiling water and kept in 95°C oven	30 min	HPLC-PO-CL	0.38[g] LOQ = 0.57	--	0.13±0.01 and 0.16±0.02[gh]
	2 new bottles (4 runs/bottle), 3rd use	Water (purity not stated)	Filled with boiling water and kept in 95°C oven	30 min	HPLC-PO-CL	0.38[g] LOQ = 0.57	--	0.14±0.01 and <LOQ[gh]
	2 new bottles (4 runs/bottle), 4th use after cleaned with a brush	Water (purity not stated)	Filled with boiling water and kept in 95°C oven	30 min	HPLC-PO-CL	0.38[g] LOQ = 0.57	--	0.18±0.02 and <LOQ[gh]
Mountfort *et al*., 1997	New bottles (n not stated) after chemical sterilization and rinsing with water for 3, 10 and 20 cycles	Commercial infant feed formula	Not stated, heated in microwave for 30 seconds	20 min	HPLC-FL	30[i]	<LOD	--
	Not described	Distilled water	40	10 days	HPLC-FL	30[i]	<LOD	--

-- Not reported

[a] Migration was reported by Li *et al*. as mean amount BPA (ng) ± standard deviation in four different brands of 240 ml bottles. For the sake of comparison in this table migration levels have been transformed into ng/ml (i.e. µg/l) and the range presented for each time point (24h; 3 days; 5 days; 7 days) represents the range of means for the different brands.

[b] Reported as "average" migration. No standard deviations reported.

[c] polycarbonate bottles washed in "domestic dishwasher" once daily for six consecutive days. Migration was analyzed before every washing cycle. BPA migration decreased abruptly from around 0.07 µg/l after the second washing and remained constant at low levels, around 0.1 µg/l.

[d] Ranges of average results for 18 bottles from the 3 time points (new; used and washed one time; used and washed two times).

[e] Same bottles that had previously been subjected to 10 cycles in dishwasher and 10 cycles of brushing with detergent.

[f] Range of average migration from bottles after each cycle. Last couple of cycles generally showing lower and <LOD levels

[g] Reported as ppb and converted here assuming a density of 1 g/ml

[h] BPA was below LOD but could be quantified when samples were evaporated in larger volumes, hence the reported levels are below LOD

[i] Reported as 0.03 mg/kg and converted here assuming a density of 1 g/ml

Table 3. Migration of BPA into water from reusable polycarbonate drinking bottles reported in the published literature.

Study	Samples	Incubation temperature (°C)	Incubation time	Method of analysis	LOD (µg/l)	BPA migration (µg/l)	
						Range	Mean
Cao and Corriveau, 2008	2 new bottles	Filled with boiling water and left at room temp	24h	GC-MS	0.05	1.7 and 4.1	--
Le *et al*., 2008	3 new bottles (3 replicates/bottle)	Filled with water (temp not stated) and left at room temp	1, 3, 5 and 7 days	ELISA	0.05	1d: 0.08 – 0.36[a] 3d: 0.25 – 0.79 5d: 0.28 – 0.68 7d: 0.73 – 1.33	--
	5 used bottles (3 replicates/bottle)	Filled with water (temp not stated) and left at room temp	1, 3, 5 and 7 days	ELISA	0.05	1d: 0.21 – 0.29[ab] 3d: 0.33 – 0.76[b] 5d: 0.29 – 0.72[b] 7d: 0.34 – 0.93	--
	2 new bottles after heating (3 replicates/bottle)	Filled with boiling water and left at room temp	24 h	ELISA	0.05	--	3.84 ± 0.12 7.67 ± 0.57
	1 used bottle after heating (3 replicates/bottle)	Filled with boiling water and left at room temp	24 h	ELISA	0.05	--	1.92 ± 0.40
	2 new bottles into room temp water after 1 use with boiling water (3 replicates/bottle)	Filled with room temp water and left at room temp	24 h	ELISA	0.05	--	2.3 ± 0.44 4.6 ± 0.59
	1 used bottle into room temp water after 1 use with boiling water (3 replicates)	Filled with room temp water and left at room temp	24 h	ELISA	0.05	--	0.66 ± 0.01
Kubwabo *et al*., 2009	5 new bottles	40	2, 8, 24, 96 and 240 h	GC-MS/MS	$4x10^{-5}$	0.01 – 2.16[c]	--
	5 new bottles	4	24 h	GC-MS/MS	$4x10^{-5}$	--	≈0.01[d]
	10 used bottles	40	24 h	GC-MS/MS	$4x10^{-5}$	--	0.20[c]
	1 used bottle	4	24 h	GC-MS/MS	$4x10^{-5}$	--	--

-- Not reported

[a] Range of mean migration from 3 replicate experiments for each bottle.

[b] Measurements from some bottles not available at this time point.

[c] Average concentrations as reported in text.

[d] Average as interpreted from figure.

Table 4. BPA-concentrations in canned food products reported in the published literature.

Study	Product	Number of samples	Method of analysis	LOD (µg/kg)	BPA concentration (µg/kg)	
					Range	Mean
Cao *et al*., 2010a	Tuna fish	15 (from 4 brands)	GC-MS	0.6	9-534	137
	Condensed soup	29	GC-MS	0.6	4.1-189	105
	Ready-to-serve soup	12	GC-MS	0.6	9.6-34	15
	Vegetables	15 (from 7 brands)	GC-MS	0.6	4.3-92	20
	Tomato paste	6 (from 4 brands)	GC-MS	0.6	<LOD-2.1	1.1
Geens *et al*., 2010	Fruits, vegetables, soups, fish, meat	27	GC-MS	LOQ=0.1	0.2-169	40.3
Rastakari *et al*., 2010	Tomato paste	12	GC-MS	0.1	<LOD-5.12	--
	Corn	12	GC-MS	0.1	<LOD-5.16	--
Lim *et al*., 2009	Tuna fish	8	HPLC-FL	3 (solids) 2 (liquids)	<LOD-117	43.7
	Fish	11	HPLC-FL	3 (solids) 2 (liquids)	<LOD-125	39.8
	Fruits	9	HPLC-FL	3 (solids) 2 (liquids)	<LOD-54.6	8.6
	Vegetables	12	HPLC-FL	3 (solids) 2 (liquids)	<LOD-21.5	3.1
	Meats	13	HPLC-FL	3 (solids) 2 (liquids)	<LOD-98.3	24.5
Pérez-Bendito *et al*., 2009	Fish	4	LC-FL	9	20-129	--
	Meat	2	LC-FL	9	<LOD-37	--
Grumetto *et al*., 2008	Peeled tomatoes	42	RP-HPLC-FL	1.1	<LOD-115	--
Yonekubo *et al*., 2008	Fish	21	LC-MS	0.3[a]	<LOD-30	--
	Vegetables	7	LC-MS	0.3[a]	<LOD-25	--
	Sauces	8	LC-MS	0.3[a]	1-235	--

Sajiki *et al.*, 2007	Fish	7	LC-ECD	0.2[a]	1-23	--
	Meat	5	LC-ECD	0.2[a]	4-20	--
	Fruits and vegetables	16	LC-ECD	0.2[a]	<LOD-78	--
	Soups and sauces	18	LC-ECD	0.2[a]	<LOD-842	--
Braunrath *et al.*, 2005	Vegetables	6	HPLC-FL	1.1-7.4[b]	8.5-35	--
	Fruits	4	HPLC-FL	1.2-5.4[b]	5-24	--
	Fat-containing products	9	HPLC-FL	0.2-9.3[b]	4.8-17.6	--
Munguia-Lopez *et al.*, 2005	Tuna fish (in oil)[c]	9 (from 3 brands)	RP-HPLC-FL	5 LOQ=7.1	<LOQ-102.7	--
Thomson *et al.*, 2005	Vegetables	16	GC-MS	LOQ=10	<LOQ-23	--
	Fruits	16	GC-MS	LOQ=10	<LOQ	--
	Fish	8	GC-MS	LOQ=20	<LOQ-109	--
	Soup and sauces	8	GC-MS	LOQ=10 (<1% fat) LOQ=20 (>1% fat)	<LOQ-21	--
	Meat	6	GC-MS	LOQ=20	<LOQ-98	--
	Spaghetti and baked beans	8	GC-MS	LOQ=10	<LOQ	--
	Infants foods	7	GC-MS	LOQ=10	<LOQ	--
	Desserts and coconut cream	5	GC-MS	LOQ=10 (<1% fat) LOQ=20 (>1% fat)	<LOQ-192	--
Goodson *et al.*, 2002	Fish	10	GC-MS	2	<LOD-44	--
	Vegetables	10	GC-MS	2	9-48	--
	Soup	10	GC-MS	2	<LOD-21	--
	Desserts	5	GC-MS	2	<LOD-14	--
	Fruit	2	GC-MS	2	19-38	--
	Infant formula	4	GC-MS	2	<LOD	--

	Pasta	5	GC-MS	2	<LOD-11	--
	Meat	5	GC-MS	2	16-422	--
Yoshida *et al.*, 2001	Vegetables and fruit	14 (from 12 brands)	HPLC-UV	LOQ=10	<LOQ-95.3	--

-- Not reported

[a] Reported as ng/ml and converted here assuming a density of 1g/ml

[b] Different LODs for different products within each category

[c] Also tested the effect of thermal processing and storage time using cans with different types of coating and fatty food simulant

Table 5. BPA –concentrations in canned beverages reported in the published literature.

Study	Product	Number of samples	Method of analysis	LOD (µg/l)	BPA concentration (µg/l)	
					Range	Average
Cao *et al*., 2010b	Soft drinks	10	GC-MS	0.0045	0.019-0.21	--
	Beer	8	GC-MS	0.0045	0.081-0.54	--
Geens *et al*., 2010	Soft drinks, energy drinks, beer, iced tea, juices	45	GC-MS	LOQ=0.02	<LOQ-8.10	1.01
Cao *et al*., 2009a	Different carbonated drinks, energy drinks and iced tea	72	GC-MS	0.045[a]	0.032-4.5	0.57
Lim *et al*., 2009	Coffee	5	HPLD-FL	2[b]	11.7-136	45.5
	Tea	3	HPLD-FL	2[b]	<LOD-14.3	8.3
Braunrath *et al*., 2005	Soft drinks, energy drinks and beer	7	HPLC-FL	0.1-0.9	<0.9- 3.4	n.a.
Thomson *et al*., 2005	Soft drinks	4	GC-MS	LOQ=10[b]	<LOQ	--
Goodson *et al*., 2002	Different carbonated soft drinks, ales, ciders and beers	11	GC-MS	2[b]	<LOD	--

-- Not reported

[a] Average LOD. LOD varied between products from 0.024-0.074µg/l

[b] Reported as µg/kg and converted here assuming a density of 1g/ml

Table 6. BPA – concentrations in human breast milk reported in the published literature.

Study	Samples	Method of analysis	LOD (ng/ml)	Free BPA (µg/l)		Total BPA (µg/l)	
				Range	Mean	Range	Mean
Otaka *et al.*, 2003	3 samples provided by volunteers in Japan	GC-MS	0.09[a]	--	--	<LOD – 0.7[a]	--
Sun *et al.*, 2004	Samples from 23 healthy mothers in Japan	HPLC-FL	0.11	--	--	0.28 – 0.97	0.61 ± 0.2
Ye et a., 2006	20 samples, presumably from the USA	SPE-HPLC-MS/MS	0.28	<LOD – 6.3	1.3	<LOD – 7.3	1.9
Kuruto-Niwa *et al.*, 2007	Samples of colostrum from 101 healthy mothers in Japan collected within 3 days of giving birth	ELISA	0.3	--	--	1-7	3.41 ± 0.13
Ye *et al.*, 2008	Samples from 4 anonymous women, presumably from the USA, without known occupational exposure to BPA	SPE-HPLC-MS/MS	0.3	0.45 – 1.54	--	0.73 – 1.62	--
Yi *et al.*, 2010	Samples from 100 volunteers in Korea within 2 weeks after giving birth	HPLC-FL	0.6	<LOD	--	<LOD – 87.7	--
		LC-MS/MS	0.39	0.65 – 29.9	6.6[b]	0.65 – 42.6	10.4[b]

-- Not reported

[a] Reported in ng/g and converted here assuming a density of 1 g/ml

[b] Median

Table 7. BPA-concentrations in air and dust reported in the published literature.

Study	Sample	Study conditions	Method of analysis	LOD (ng/m^3; air) (ng/g; dust)	BPA concentrations in air (ng/m^3) and dust (ng/g)	
					Range	Mean
Matsumoto *et al*., 2005	Outdoor air	Samples collected from urban outdoor air in Osaka, Japan over six months using high-volume air sampler on rooftop.	GC-MS	0.01	0.01 – 1.92	0.51
Wilson *et al*., 2007	Outdoor air	Samples collected from air outside homes of 257 preschool children in Ohio and North Carolina	GC-MS	0.9	<LOD – 44.6	--
	Outdoor air	Samples collected from air outside daycare centers of 257 preschool children in Ohio and North Carolina	GC-MS	0.9	<LOD – 51.5	--
	Indoor air	Samples collected from air inside homes of 257 preschool children in Ohio and North Carolina	GC-MS	0.9	<LOD – 193	--
	Indoor air	Samples collected from air inside daycare centers of 257 preschool children in Ohio and North Carolina	GC-MS	0.9	<LOD – 8.99	--
	Dust	Samples collected from homes of 257 preschool children in Ohio and North Carolina using a vacuum sampler	GC-MS	20	<LOD – 707	--
	Dust	Samples collected from daycare centers of 257 preschool children in Ohio and North Carolina using a vacuum sampler	GC-MS	20	<LOD – 156	--
Völkel *et al*., 2008	Dust	Samples collected from 12 homes in Bavaria, Germany by the residents using regular vacuum cleaners	LC-MS/MS	--	117-1486	553
Geens *et al*., 2009	Dust	Samples collected from 18 homes in Belgium using a vacuum cleaner	LC-MS/MS	LOQ = 0.5	535 – 9729	2001
	Dust	Samples collected from 2 offices in Belgium using a vacuum cleaner	LC-MS/MS	LOQ = 0.5	4685 and 8380	--
Loganathan and Kannan, 2011	Dust	Samples collected from 50 homes and 6 labs in the Eastern U.S. using vacuum cleaners	HPLC-MS/MS	0.5	<LOD – 10200	843

-- Not reported

Table 8. BPA-concentrations maternal and fetal blood and amniotic fluid reported in the published literature.

Study	Samples	Analytical method	LOD (µg/L)	BPA concentration (µg/L), median (range) or mean±std		
				Serum/plasma		Amniotic fluid
				Maternal	Fetal	
Lee *et al*., 2008	Maternal and umbilical cord blood (serum) from 300 Korean women	HPLC-FD (validated by GC-MS and LC-MS)	0.625	2.73 (n.d. - 66.48) 9.04 ± 14.03	<LOD (n.d. – 8.86) 1.13 ± 1.43	--
Ikezuki *et al*., 2002	Maternal blood (serum) from women in "early pregnancy" (n=37) and "late pregnancy" (n=37), umbilical cord blood (serum) at full term (n=32), amniotic fluid at 15-18 weeks of gestation (n=32) and at full-term (n=38). Unclear if the different types of samples were collected from the same subjects.	ELISA	0.5	"early pregnancy": 1.5 ± 1.2 "late pregnancy": 1.4 ± 0.9	2.2 ± 1.8	15-18 weeks: 8.3 ± 8.9 Full term: 1.1 ± 1.0
Schönfelder *et al*., 2002	Maternal and umbilical cord blood (plasma) from 37 Caucasian females in Berlin, Germany	GC-MS	0.01	3.1 (0.3 – 18.9) 4.4 ± 3.9	2.3 (0.2 – 9.2) 2.9 ± 2.5	--
Yamada *et al*., 2002	Maternal blood (serum) and amniotic fluid at early second trimester from 200 women carrying fetuses with normal karyotypes.	ELISA	0.2	2.24 (0.63 – 14.36)	--	0.26 (<LOD – 5.62)
	Maternal blood (serum) and amniotic fluid at early second trimester from 48 women carrying fetuses with abnormal karyotypes.	ELISA	0.2	2.97 (1 – 18)*	--	0 (<LOD – 7)*

n.d. not detected

-- not reported

* range not reported, estimated from figure

Appendix I

Applications of BPA based on data on global production volumes from 2005 and 2006, as reported by industry (Plastics Europe, 2007).

POLYCARBONATE
66% of total BPA production

Optical media (32% of total polycarbonate production)

- CDs
- CD-ROMs
- DVDs
- HD-DVDs
- Blue-Ray discs
- Holography discs
- Innovative data storage technology (e.g. near field recording discs)
- Forgery-proof holographic shadow pictures in ID cards

Electrical and electronics (23% of total polycarbonate production)

- Housings for cell phones, SLR cameras, electrical razors, hairdryers, steam irons, mixers, computers, monitors, TVs, copiers, printers, telephones, microwaves, coffee makers
- Front panels for electric cookers
- Electrical kettles
- Transparent front panels for vending machines
- Interior lighting panels for trains and air planes
- Backlight units for TVs
- Housing for switch modules, distributer boxes, fuses, battery power stations, sockets, electrical meters
- Illuminated rotary switches
- Switches
- Plug connectors, plugs
- Lamp holders

Construction (13% of total polycarbonate production)

- Sheets for roofing, conservatory glazing
- Architectural glazing(e.g. sports arenas)
- Greenhouse glazing
- Roof lights
- Cover for solar panels
- Noise reduction walls for roads and train tracks
- Carport covers
- Glazing for bus stop shelters

- Road signs
- Internal safety shields for stadiums
- Transparent cabins for ski lifts
- Housings and fittings for halogen lighting systems
- Front panels for advertising posters and signboards (e.g. fuel stations
- Large advertising displays
- Dust& water-proof luminairs for streetlights and lamp globes
- Diffusing reflectors for traffic lights

Automotive (9% of total polycarbonate production)

- Fixed side windows
- Transparent and retractable roof modules
- Windstops in convertibles
- Rear windows
- Transparent rear body parts
- Headlamp lenses
- Headlamp, tail light, indicator reflectors
- Fog lamps
- Interior light covers
- High-mount brake lights
- Housings for license-plate lights
- Bumpers
- Radiator grills
- Dashboards

Bottles and packaging (3% of total polycarbonate production)

- Reusable water bottles
- Unbreakable baby bottles
- Reusable milk bottles
- Cutlery
- Food containers (plates, glasses, bowls)
- Drinking water generators

Medical and health care (3% of total polycarbonate production)

- Blood oxygenators
- Cardiotomy reservoirs
- Dialysers
- Respirators
- Dentists´ operating lamps
- Safety valves for respirators
- Breast pumps
- Inhaler housings
- Prescription spectacles
- i.v. connectors
- Scalpel cases
- Laparoscope handles

- Contact lens holders
- Syringe tops
- Medical packaging film
- Ampoules
- Three-way stop cocks and stop cocks Manifolds
- Tweezers with integrated lighting
- Single-use operating instruments

Others (2% of total polycarbonate production)

- Safety goggles
- Protective visors for welding or handling of hazardous substances
- Protective visors for motorbikes, snowmobiles
- Motorbike and cycle helmets
- Fencing helmets
- Safety shields for policemen
- Guards to protect workers from moving machine parts
- Ski goggles
- Sun glasses
- Transparent building blocks in toys
- Mouth pieces for musical instruments
- Compass housings
- Binocular housings
- Seats for sleighs
- Ballpoint pen casings
- Transparent roof modules in caravans
- Instrumentation housings in boats
- Suitcase shells

Blends (15% of total polycarbonate production)

Mainly used in automotive and electrical and electronics

EPOXY

30 % of total BPA production

Marine and protective coatings (20% of total epoxy production)

- Water ballast tanks
- Under water ship hulls
- Cargo tank linings
- Offshore oil drilling platforms
- Supporting steel structures
- Sea containers
- Steel bridges
- Storage tanks (metal and concrete)
- Power plant scrubbers
- Electric motors, engines, machinery
- Drinking water distribution pipes (metal and concrete)

- Gas pipes

Powder coatings (18% of total epoxy production)

- Construction panels (cladding, metal roofing, ceiling, garage doors)
- Radiators
- Rebars (concrete reinforcement)
- Gardening tools& equipment
- Engine blocks
- Automotive parts
- Steel furniture
- Steel racks, frames, beds
- Office furniture(shelves, metal desks, filing cabinets)
- Pipes, valves & fittings

Electrical and electronics (16% of total epoxy production)

- Potting/encapsulation electronic parts (transformers, inductors)
- Printed circuit boards

Civil engineering (15% of total epoxy production)

- Flooring (industrial/public buildings, food/catering industry, chemical plants, pharmaceutical industry, hospitals)
- Mortars, grouting (tile& brick linings)
- Fillers, crack repair
- Coatings concrete bridges (seal against water and de-icing chemicals)
- Coating secondary containment walls (groundwater protection)
- Anti-skid coatings for park decks

Can and coil coatings (11% of total epoxy production)

- Food and drink cans/can ends
- Menu trays, food trays
- Caps& closure, crown corks
- Drums, pails
- General line cans (oil, hairspray)
- Collapsible tubes (toothpaste, cream)
- Construction panels(cladding, metal roofing, ceilings, garage doors)
- Cookers
- Mobile homes, caravans
- Heat, ventilation, Air Conditioning equipment
- Office furniture(metal desks, shelves, filing cabinets, cupboards)
- Fridges and freezers
- Dishwashers, washing machines, dryers
- Household appliances (e.g. vacuum cleaners)

Automotive coatings (9% of total epoxy production)

- Water borne primers for cars, buses, rail cars

Composites (5% of total epoxy production)

- Rackets (tennis, badminton, squash), hockey sticks and golf clubs
- Ski, ski poles, snowboards
- Surfboards
- Boats, canoes
- Hang gliders
- Helmets
- Light weighing bicycles
- Pipes, valves and fittings
- Storage tanks, containers, gas bottles
- Windmill blades
- Scrubbers
- Pultruded structural parts (rods, bars, shafts, beams, grating)
- Car parts (body panels, cabin, spoiler, leaf springs, drive shafts)
- Railcars, boats, yachts
- Aviation (aircraft), aerospace, military (helicopters)

Adhesives (4% of total epoxy production)

- Do-it-yourself repair kits (adhesives, fillers)
- Structural adhesives for buildings and construction
- Adhesives for cars, boats, aircraft

Photocure (2% of total epoxy production)

- Printing inks
- Wood coating
- Paper and board varnish, incl. food packaging
- Coating for plastics and primed metals

OTHER RESINS

2% of total BPA production

TBBPA

2% of total BPA production

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